Paper 59

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UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

HORNG-CHIH HUANG and DAVID B. REITZ,
Junior Party,

(Application 08/541,850),

v.

PETIBOON PRASIT, DANIEL GUAY, ZHAOYIN WANG,
SERGE LEGER, and MICHAEL THERIEN,
Senior Party,

(Application 08/793,931).

Patent Interference No. 104,134

Before: McKELVEY, Senior Administrative Patent Judge, and SCHAFER, LEE, and GARDNER-LANE, Administrative Patent Judges.

GARDNER-LANE, Administrative Patent Judge.

FINAL DECISION AND JUDGMENT

I. Introduction

An oral argument was held on 4 December 2000 on:

(1) the Huang request for reconsideration of the decision denying Huang preliminary motion 1 and

(2) priority

A. Findings of fact

The record supports, by a preponderance of the evidence, the following findings, as well as any findings set out in the discussion portion of this ORDER.

The interference

1. The interference involves a Huang application versus a Prasit application.

Junior party

2. The junior party is Horng-Chin Huang and David B. Reitz ("Huang").

3. Huang is involved in the interference on the basis of its U.S. application 08/541,850("'850"), filed 10 October 1995.

4. Huang has not been accorded the benefit of the filing date of any other application for the purpose of priority.

5. The real party in interest is G.D. Searle and Company ("Searle"). Searle is said to be a wholly-owned

subsidiary of Pharmacia Corporation (formerly Monsanto Company) (Paper 47 at i).

Senior party

6. The senior party is Petpiboon Prasit, Daniel Guay, Zhaoyin Wang, Serge Leger, and Michel Therien ("Prasit").

7. Prasit is involved on the basis of its U.S. application 08/793,931 ("'931"), filed 25 February 1997.

8. For the purpose of priority, Prasit has been accorded the benefit of the filing dates of (Paper 1 at 14):

(1) PCT application PCT/CA95/00490, filed 24 August 1995

(2) U.S. application 08/297,461, filed 29 August 1994

9. The real party in interest is Merck & Company, Inc. ("Merck").

The count

10. The count is the interference is as follows (Paper 1 at 15):

A compound according to claim 1 of the Huang application,

or

a pharmaceutical composition according to claim 12 of the Huang application,

or

a method according to claim 13 of the Huang application,

or

a compound according to claim 24 of the Prasit application,

or

a pharmaceutical composition according to claims 15-16 of the Prasit application,

or

a method according to claims 17-18 of the Prasit application.

11. The count can be summarized as being the first compound set out below (the Huang claim 1 compound), or the second compound set out below (the Prasit claim 24 compound), a pharmaceutical composition containing either of the compounds, or a method of treating inflammatory diseases or cyclooxygenase mediated diseases with either of the compounds.

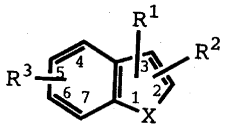
The Huang compound:

A compound of the formula:

X is O or S;

wherein R^1 is selected from aryl and heteroaryl; wherein R^1 is optionally substituted with one or more radicals selected from halo, alkylthio, alkylsulfinyl, alkyl, alkylsulfonyl, cyano, carboxyl, alkoxycarbonyl, aminocarbonyl, N-alkylaminocarbonyl, N-arylamino-carbonyl, N,N-dialkylaminocarbonyl, N-alkyl-N-arylaminocarbonyl, haloalkyl, hydroxyl, alkoxy, hydroxyalkyl, haloalkoxy, amino, N-alkylamino, N,N-dialkylamino, nitro and alkylcarbonylamino,

wherein R^2 is aryl substituted with a radical selected from alkylsulfonyl and aminosulfonyl; and

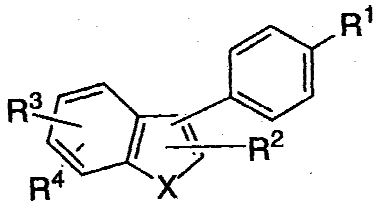


wherein R^3 is one or more radicals selected from hydrido, halo, alkyl, and haloalkyl;

or a pharmaceutically-acceptable salt thereof.

The Prasit compound:

A compound of the formula



or a pharmaceutically acceptable salt thereof wherein:

X is O or S,

R^1 is selected from the group consisting of

(a) $S(O)_2CH_3$,

(b) $S(O)_2NH_2$,

(c) $S(O)_2NHCOCF_3$,

(d) $S(O)(NH)CH_3$,

(e) $S(O)(NH)NH_2$,

(f) $S(0)(NH)NHCOCF_3$,

(g) $P(O)(CH_3)OH$, and

(h) $P(O)(CH_3)NH_2$,

R^2 is selected from the group consisting of

(a) C_{1-6} alkyl,

(b) C_{3-7} cycloalkyl,

(c) mono- or di-substituted phenyl or napthyl wherein the substituent is selected from the group consisting of

(1) hydrogen,

(2) halo, including F, Cl, Br, I,

(3) C_{1-6} alkoxy,

(4) C_{1-6} alkylthio,

(5) CN,

(6) CF_3,

(7) C_{1-6} alkyl,

(8) N_3,

(9) $-CO_2H$,

(10) $-CO_2-C_{1-4}$ alkyl,

(11) $-C(R^5)(R^6)-OH$,

(12) $-C(R^5)(R^6)-O-C_{1-4}$ alkyl, and

(13) $-C_{1-6}$ alkyl$-CO_2-R^7$;

(d) mono- or di-substituted heteroaryl wherein the heteroaryl is a monocyclic aromatic ring of 5 atoms, said ring having one hetero atom which is S, O, or N, and optionally 1, 2, or 3 additional N atoms; or the heteroaryl is a monocyclic ring of 6 atoms, said ring having one hetero atom which is N, and optionally 1,2,3, or 4 additional N atoms; said substitutents are selected from the group consisting of

(1) hydrogen,

(2) fluoro, chloro, bromo and iodo,

(3) C_{1-6} alkyl,

(4) C_{1-6} alkoxy,

(5) C_{1-6} alkylthio,

(6) CN,

(7) CF_3,

(8) N_3,

(9) $-C(R^5)(R^6)-OH$, and

(10) $-C(R^5)(R^6)-O-C_{1-4}$ alkyl;

(e) benzoheteroaryl which includes the benzo fused analogs of (d);

R^3 and R^4 are independently selected from the group consisting of:

(a) hydrogen,
(b) CF_3,
(c) CN,
(d) C_{1-6} alkyl,
(e) Q^1 wherein Q^1 is Q^2, CO_2H, $C(R^5)(R^6)OH$,
(f) $-O-Q^2$,
(g) $-S-Q^2$, and
(h) optionally substituted
(1) $-C_{1-5}$ alkyl-Q^1,
(2) $-O-C_{1-5}$ alkyl-Q^1,
(3) $-S-C_{1-5}$ alkyl-Q^1,
(4) $-C_{1-3}$ alkyl-$O-C_{1-3}$ alkyl-Q^1,
(5) $-C_{1-3}$ alkyl-$S-C_{1-3}$ alkyl-Q^1,
(6) $-C_{1-5}$ alkyl-$O-Q^2$,
(7) $-C_{1-5}$ alkyl-$S-Q^2$,

wherein the substituent resides on the alkyl chain and the substituent is C_{1-3} alkyl, and

Q^1 is Q^2, CO_2H, $C(R_5)(R_6)OH$

Q^2 is CO_2-C_{1-4} alkyl, tetrazolyl-5-yl, or $C(R^5)(R^6)O-C_{1-4}$ alkyl;

R^5, R^6 and R^7 are each independently selected from the group consisting of

(a) hydrogen,
(b) C_{1-6} alkyl

or R^5 and R^6 together with the carbon to which they are attached form a saturated monocyclic carbon ring of 3, 4, 5, 6, or 7.

12. All the claims of the '850 application and all the claims of the '931 application correspond to the count (Paper 1 at 15).

General explanation of the involved technology

13. The Huang and Prasit compounds are said to be selective cyclooxygenase-2 ("COX-2") inhibitors.

14. The '850 specification and the '931 specification each contain a general explanation of the technology as summarized below ('850 at 1-2 and '931 at 1-2).

15. The formation of prostaglandins in the body is believed to be catalyzed, in part, by the enzyme cyclooxygenase. Prostaglandins have been implicated in tissue inflammation.

16. It is believed that cyclooxygenase inhibitors function as anti-inflammatory agents by inactivating the enzymatic activity of cyclooxygenase.

17. There are at least two types of cyclooxygenase inhibitors, i.e., COX-1 inhibitors and COX-2 inhibitors.

18. COX-2 inhibitors are believed to have the same anti-inflammatory effect as COX-1 inhibitors; however, COX-2 inhibitors seem to have fewer and less severe negative gastrointestinal side effects (e.g., ulcer formation) than COX-1 inhibitors.

Huang request for reconsideration of the denial of Huang preliminary motion 1

19. Huang preliminary motion 1 was denied in an order entered 23 December 1999 (Paper 35).

20. Huang asks for reconsideration of the denial of its preliminary motion 1. 37 CFR § 1.655(a)(Paper 47).

21. Huang argues that the Prasit claims are unpatentable under 35 U.S.C. §§ 101 or 112, 1st paragraph, on the basis of what is said to be an admission against interest made by Merck in copending interferences 103,845 ("'845") and 103,873 ("'873").

22. According to Huang, Merck, the real party interest of Prasit, made an admission that *in vitro* testing alone is insufficient to make reliable predictions concerning *in vivo* effectiveness in compounds alleged to possess anti-inflammatory, antipyretic, and analgesic activity.

23. The following testimony by Merck witnesses during the '845 and '873 interferences is said to be evidence of the Merck admission:

(a) the testimony of Dr. Chi-Chung Chan that:

(1) *"In vitro* inhibition of COX-2 is necessary, but considered alone, is not sufficient to make reliable predictions concerning *in vivo* effectiveness of compounds and takes no account of

absorption, distribution, metabolism and excretion, all of which affect the activity of a compound *in vivo*"
(Exh. 2002 at ¶15); and

(2) "...*in vitro* activity alone is not a reliable predictor of *in vivo* activity" (Exh. 2002 at ¶26).

(b) the testimony of Dr. Denis Riendeau that:

(1) *"In vitro* inhibition of COX-2 is necessary, but considered alone, is not sufficient to make reliable predictions concerning *in vivo* effectiveness of compounds and takes no account of absorption, distribution metabolism and excretion, all of which affect the activity of a compound *in vivo"* (Exh. 2003 at ¶17); and

(2) "I also believe that activity in an *in vitro* assay is not sufficient to make reliable predictions concerning *in vitro* effectiveness of compounds and takes no account of absorption, distribution, metabolism and excretion, all of which affect the activity of a compound *in vivo"* (Exh. 2003 at ¶27).

24. The Prasit application contains no *in vivo* data demonstrating the efficacy of the compounds Prasit claims.

25. Huang disagrees with Merck's admission but argues that Merck should be held to its prior admission and should not be able to take a position in this interference that is contrary to the position it took in the '845 and '873 interferences

(Paper 47 at 4).

26. Both Dr. Chang and Dr. Riendeau testified that their views were reached after "carefully stud(ying)" applications 08/004,822 and 08/425,029 (applications involved in the '845 and '873 interferences).

27. At a point in his testimony prior to his testimony set out at FF[1] 22, Dr. Chang testified (Exh. 2002 at ¶7):

> I have carefully studied the Bertenshaw Applications USSN 08/004,822 (DE 62), USSN 08/425,029 (DE 61, pages 0146-0233) and the Declaration on behalf of Ducharme of Dr. Denis Riendeau (DE 16) and based on the study I have found the following:

28. At a point in his testimony prior to his testimony set out at FF 22, Dr. Riendeau testified (Exh. 2003 at ¶9):

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[1] Finding of Fact.

I have carefully studied, the Bertenshaw Application USSN 08/425,029 (DE 61, pages 0146-0233), and *in vitro* assays used therein, and the Declaration for Ducharme of Dr. A. Jerry Kresge (DE 6), and based on that study I have found the following:

29. Huang argues that the testimony of the Merck witnesses relate to problems with *in vitro* testing in general and is applicable to all compounds regardless of their structure (Paper 47 at 6).

30. Huang argues that Merck should be bound by its admissions in the '845 or '873 interferences under principles of judicial estoppel (Paper 47 at 6).

Priority

31. Prasit relies upon the 29 August 1994 filing date of its benefit application, 08/297,461. Prasit argues that Huang has not established a date of invention prior to the 29 August 1994 filing date (Paper 49 at 1).

32. Huang argues that it "has established a date of invention, i.e., an actual reduction to practice, of the subject matter defined by the interference count at least as early as September 28, 1993" (Paper 46 at 1).

33. According to Huang, on 2 September 1993, inventor Dr. Horng-Chih Huang entered, in his notebook,

evidence of a conception of compounds falling within the scope of the count as having utility as COX-2 inhibitors (Exh. 2009).

34. Dr. David B. Reitz, an inventor, testified that he witnessed the Huang notebook entry (Exh. 2009 and Exh. 2020 at ¶4).

35. Dr. Reitz testified that, on 4 September 1993, he synthesized a compound said to be 2-[4-(methylthio)phenyl] benzofuran (Exh. 2020 at ¶5), as a starting material for synthesizing compounds falling within the scope of the Huang conception (FF 33), and entered the synthesis procedure in his notebook (Exh. 2014).

36. Dr. James J. Li testified that he witnessed the notebook entry of Dr. Reitz on 7 September 1993 (Exh. 2025 at ¶4).

37. Dr. Huang testified that, on 8-9 September 1993, he synthesized 3-(4-fluorophenyl)-2-[4-(methylsulfonyl)phenyl] benzofuran (Exh. 2018 at ¶4), a compound falling within the scope of the count, and entered the synthesis procedure in his notebook (Exh. 2010). According to Huang, the compound was assigned the Searle Compound ("SC") identification SC-58394 and is claimed in claim 5 of the '850 application (Exh. 2018 at ¶9 and Paper 46

at 7).

38. Dr. Jacob S. Tou testified that he witnessed the notebook entry of Dr. Huang on 16 September 1993 (Exh. 2026 at ¶¶3-4).

39. According to Huang, NMR analysis confirmed the structure of the products obtained by Dr. Reitz and Dr. Huang (Exh. 2011 at 2-10 and Exh. 2020 at ¶7).

40. According to Huang, elemental analysis (Exh. 2013) and mass spectroscopy (Exh. 2012) confirmed the production and recovery of 3-(4-fluorophenyl)-2-[4-methylsulfonyl)phenyl] benzofuran (Exh. 2018 at ¶¶7-8; Exh. 2021 at ¶¶2-4; and Exh. 2024 at ¶¶2-5). Dr. Huang testified that he provided a sample of SC-58394 to Monsanto employee, Carol M. Koboldt for "biological testing" (Exh. 2018 at ¶9).

41. Subsequent to the Dr. Reitz and Dr. Huang syntheses, Huang states that other syntheses of compounds within the scope of the count were undertaken by Searle employee,
Dr. Timothy Chamberlain at the instruction of Dr. Reitz. According to Dr. Chamberlain, he was asked by Dr. Reitz to synthesize several diphenybenzofurans for testing of their anti-inflammatory activity as COX-2 inhibitors (Exh. 2019 at ¶2).

Dr. Chamberlain testified that he confirmed the structure of each compound by biological tests, including NMR analysis, elemental analysis, and mass spectroscopy (Exh. 2019 at ¶¶5-15, Exh. 2022, and Exh. 2023). Below is a list of the compounds said to be within the scope of the count and said to have been synthesized by Chamberlain in February and March of 1994 along with the SC identification of each (Paper 46 at 7-12):

(1) 4-[3-(4-fluorophenyl)-benzofuran-2-yl] benzenesulfonamide
(SC-60246)

(2) 3-(3-chloro-4-methoxyphenyl)-2-[4-(methylsulfonyl)phenyl]benzofuran
(SC-60247)

(3) 3-(3-fluoro-4-methoxyphenyl)-2-[4-(methylsulfonyl)phenyl]benzofuran
(SC-60248)

(4) 4-[3-(3-fluoro-4-methoxy phenyl)-benzofuran-2-yl]benzenesulfonamide
(SC-60667)

(5) 4-[3-(3-chloro-4-methoxyphenyl)-benzofuran-2-yl]benzenesulfonamide
(SC-60668)

Dr. Chamberlain testified that the syntheses were recorded in his notebook (Exh. 2015).

The Koboldt testing

42. Koboldt testified that, on 16 September 1993, she received material identified as SC-58394 from Dr. Henry

Huang[2] who requested that the compound be tested for anti-inflammatory activity in the Monsanto COX-1/COX-2 inhibition assay. According to Koboldt, she received material identified as SC-60246,
SC-60247, SC-60248, SC 60668, and SC-60668 from Dr. Chamberlain for testing in the assay in February and March of 1994 (Exh. 2029 at ¶¶4-6).

43. The Monsanto assay is said to be an assay that tests a compound for its ability to inhibit COX-2 selectively over COX-1 (Paper 46 at 13).

44. The Monsanto assay is an *in vitro* assay.

45. According to Koboldt, the results for each tested compound, which were recorded in her notebook (Exh. 2038), showed the compound to have selectivity for COX-2 inhibition (Exh. 2029 at ¶9). In particular, Koboldt testified that SC-58394 was tested on 20, 23, and 28 September 1993. Based on results she obtained, Koboldt testified that she expected each tested compound, including SC-58394, to have pharmacologically useful anti-inflammatory properties (Exh. 2029 at ¶¶9-14).

[2] We understand "Henry Huang" to be Dr. Horng-Chi Huang. If this is not the case, Huang should inform the Board upon receipt of this decision.

The Veenhuizen testing

46. According to Amy Veenhuizen, the compounds said to have been synthesized by Dr. Chamberlain, were sent to her by

Dr. Chamberlain for testing using the Searle one-day air pouch assay.

47. Veenhuizen testified that the air pouch assay is an *in vivo* assay for testing compounds for anti-inflammatory activity predictive of practical therapeutic utility (Exh. 2044 at ¶2).

48. Veenhuizen testified that based on the results she obtained from the air pouch assay, she expected each of the tested compounds to have pharmacologically useful anti-inflammatory activity (Exh. 2044 at ¶11).

49. Veenhuizen testified that the results were recorded in her notebook between 14 April 1994 and 4 May 1994 (Exh. 2044 at ¶¶6-10 and Exh. 2047).

The Anderson testing

50. According to Gary Anderson, compound SC-60668 was sent to him by "the COX-2 chemistry team" for testing for anti-inflammatory activity" (Exh. 2048 at ¶4).

51. Anderson's testimony does not identify the particular member or members of the "COX-2 chemistry team" who requested the testing.

52. Anderson testified that he tested the compound in an *in vivo* standard G.D. Searle arthritis assay (Exh. 2048 at ¶5).

53. Anderson testified that, based on the results of the assay, he recognized that SC-60668 had pharmacologically useful anti-inflammatory activity (Exh. 2048 at ¶6).

54. According to Anderson, he obtained the results of the arthritis assay on 9 May 1994 and recorded the results in his notebook (Exh. 2048 at ¶6).

Laura Holtzman

55. Koboldt, Veenhuizen, and Anderson each testified that the results obtained from testing were reported to Laura Holtzman for entering into the corporate data base.

56. Laura Holtzman has not testified in the interference. We have not been pointed to evidence of record that establishes that Laura Holtzman entered the test results into the corporate database.

57. We have not been pointed to evidence of record that establishes that Dr. Huang or Dr. Reitz were aware or were informed of the results of any of the testing performed

by Koboldt, Veenhuizen, or Anderson, or of any results entered into the database by Holtzman.

B. Discussion

1. The Huang request for reconsideration of the denial of Huang preliminary motion 1

In its preliminary motion 1 (Paper 25), Huang moved for judgment that all the claims of the Prasit application are unpatentable to Prasit under 35 U.S.C. §§ 101 or 112, first paragraph as lacking an adequate description of utility and failing to be supported by an enabling disclosure. Huang preliminary motion 1 was denied (Paper 35). At the request of Huang, we reconsider its preliminary motion 1. We DENY the preliminary motion.

A party filing a motion has the burden of proof to show that it is entitled to the relief sought in the motion. 37 CFR § 1.637(a). Statements in the specification regarding enablement are presumed correct unless there is reason to question the objective truth of those statements. A finding that a compound lacks utility or fails to teach how to use the invention is appropriate only if one of ordinary skill in the

art would have reasonably doubted the utility asserted. In re Cortright,
165 F.3d 1353, 1357, 49 USPQ2d 1464, 1466 (Fed. Cir. 1999). Therefore, Huang has the burden to show by a preponderance of the evidence that one having ordinary skill in the art would have doubted Prasit's assertion that the compounds it claims are useful as COX-2 inhibitors. We hold that Huang has not met its burden.

Huang argues that Merck should be bound by the testimony of its witnesses, Dr. Chan and Dr. Riendeau, given in prior interferences '845 and '873 to which Merck was a party. According to Huang, the testimony is an admission by Merck that the compounds of its '931 application lack utility and enablement.

It is proper for Huang to rely upon the testimony given by Dr. Chan and Dr. Riendeau in the '845 and '873 interferences.
37 CFR § 1.683(a). However, a review of the entire testimony of
Dr. Chan and Dr. Riendeau indicates that their testimony concerning the predictability of COX-2 inhibition from *in vitro* testing was directed to the specific compounds described

in the '822 and '029 applications. In particular, both Dr. Chan and

Dr. Riendeau testified that they reached their views with respect to the predictability of COX-2 inhibition after having "carefully studied" either or both of the '822 and '029 applications (see FF 26 and 27). Because Dr. Chan's and Dr. Riendeau's testimony was directed to particular compounds found within the disclosures of the '822 or '029 applications, we do not regard either witness' testimony as describing a general standard of predictability for COX-2 inhibition that is recognized in the art.

Huang argues that the "the Board has read too much into the declarants having 'carefully studied' the Searle applications" (Paper 47 at 5). Huang argues that nothing in the testimony of Dr. Chan or Dr. Riendeau limits their finding to any particular compound or compounds. However, Dr. Chan and Dr. Riendeau testified that their findings were based on the study of the '822 and '029 applications involved in the '845 and '873 interferences. Neither the '822 nor the '029 application discloses the compounds of the present count. Huang has not established that testimony based on the compounds disclosed in the '822 or the '029 application would be applicable to the compounds of the present count.

We also note that Huang is in disagreement with the position that *in vitro* testing alone cannot predict COX-2 inhibitory activity. Huang states that it "disagrees with Merck's admission that *in vitro* activity alone is ***not sufficient*** to make reliable predictions concerning *in vivo* effectiveness of compounds alleged to possess such anti-inflammatory, antipyretic and analgesic activity...." (Paper 47 at 4).

Huang has not met its burden by proving that a person having ordinary skill in the art would have reasonably doubted that the compounds claimed by Huang possessed COX-2 inhibitory activity.

Accordingly, we DENY Huang preliminary motion 1.

2. Priority

Prasit relies upon its earliest benefit date of 29 August 1994 for priority. Huang argues that it actually reduced to practice an embodiment of the count prior to 29 August 1994. Huang does not argue diligence. Therefore, if Huang cannot establish a reduction to practice date prior to 29 August 1994, Huang cannot prevail on priority. We hold that Huang has not established an actual reduction to practice prior to 29 August 1994.

An inventor can establish an actual reduction to practice if it is shown that: (1) the inventor constructed an embodiment or performed a process that met all the limitations of the interference count; and (2) the inventor determined that the invention would work for its intended purpose. Cooper v. Goldfarb, 154 F.3d 1321, 1327, 47 USPQ2d 1896, 1901 (Fed. Cir. 1998). Where an interference count is not limited to an intended purpose or to discovered properties of the claimed compounds, evidence establishing substantial utility for any purpose is sufficient to show reduction to practice. Fujikawa v. Wattanasin, 93 F.3d 1559, 1564, 39 USPQ2d 1895, 1899 (Fed. Cir. 1996). An alternative of the count in this interference is a compound with no limitation as to the intended utility of the compound (e.g., Huang claim 1). In the present circumstances therefore, Huang must establish that the Huang inventors actually made the invention defined by the compound alternative of the count, recognized it for what it was, and knew it would work for some practical utility. Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d 588, 592, 44 USPQ2d 1610, 1613 (Fed. Cir. 1997). When testing is required to establish utility, there must be some recognition of successful testing for a reduction to practice to have occurred. Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d at

594-595, 44 USPQ2d at 1615. Whether a practical utility has been established for a novel compound is a question of fact. Fujikawa v. Wattanasin, 93 F.3d at 1564, 39 USPQ2d at 1899.

Huang argues that neither Dr. Huang nor Dr. Reitz needed to be aware of the test results obtained by Monsanto employees Koboldt, Veenhuizen, or Anderson for a reduction to practice (Paper 51 at 20). Huang argues that the testing of the Monsanto employees inures to the benefit of Dr. Huang and Dr. Reitz. According to Huang, each of the tested compounds was reduced to practice as of the earliest date of successful testing for anti-inflammatory activity (Paper 46 at 23).

Inurement involves a claim that, as a matter of law, the acts of another accrue to the inventor for the purposes of establishing a reduction to practice. Cooper v. Goldfarb, 154 F.3d at 1331, 47 USPQ2d at 1904-05. A non-inventor's recognition of the utility of an invention can inure to the benefit of the inventor if it can be established that:

(1) the inventor conceived of the invention,

(2) the inventor had an expectation that the embodiment tested would work for the intended purpose of the invention, and

(3) the inventor submitted the embodiment for testing for the intended purpose of the invention. Genentech, Inc. v.

Chiron Corporation, 220 F.3d 1345, 1354, 55 USPQ2d 1636, 1643 (Fed. Cir. 2000).

In order to establish inurement, an inventor must show, among other things, that the non-inventor was working at the inventor's request, either explicitly or implicitly. Cooper v. Goldfarb, 154 F.3d at 1332, 47 USPQ2d at 1905.

The Koboldt, Veenhuizen, and Anderson testimony

Koboldt testified that she received "material identified as SC-58394 from Henry Huang who requested that the compound be tested for anti-inflammatory activity in the Monsanto COX-1/COX-2 inhibition assay" (Exh. 2029 at ¶4). Koboldt also testified that she received material identified as SC-60246, SC-60247, SC-60248, SC-60667 and SC 60668 from Dr. Chamberlain for testing in the COX-1/COX-2 assay.

Veenhuizen testified that she "received from Timothy Chamberlain material identified as SC-60246, SC-60247, SC-60248, SC-60667 and SC 60668 for testing for anti-inflammatory activity using the Searle one-day pouch assay" (Exh. 2044 at ¶4).

Anderson testified he "received material identified as SC-60668 from the COX-2 chemistry team for testing for anti-inflammatory activity in the G.D. Searle adjuvant arthritis assay" (Exh. 2048 at ¶4). In his testimony,

Anderson did not identify the member or members of the "COX-2 chemistry team" who requested that the testing be performed.

The Huang and Reitz testimony

Dr. Huang testified that he submitted SC-58394 to Koboldt for "biological testing" (Exh. 2018 at ¶9). Dr. Huang did not testify that he submitted any other compounds synthesized by himself or Dr. Chamberlain for testing to establish utility.

Dr. Reitz did not testify that he submitted any compound synthesized by Dr. Huang, Dr. Chamberlain, or himself, for biological testing to establish utility. Neither Dr. Huang nor Dr. Reitz testified that he directed Dr. Chamberlain to perform any syntheses or testing of compounds within the scope of the count.

The Chamberlain testimony

Dr. Chamberlain testified that he was asked by Dr. Reitz to synthesize several diphenylbenzofurans "for testing of their

anti-inflammatory activity as COX-2 inhibitors" (Exh. 2019 at ¶2); however, we have not been pointed to evidence of record that establishes that Dr. Chamberlain requested the Koboldt, Veenhuizen, or Anderson testing at the explicit or

implicit direction of the inventors. In particular, we have not been pointed to evidence of record establishing that:

(1) the diphenylbenzofuran compounds that Dr. Reitz asked Dr. Chamberlain to synthesize were the compounds tested by Koboldt, Veenhuizen, or Anderson, or

(2) that Dr. Reitz directed Dr. Chamberlain to perform, or have performed, testing to show anti-inflammatory activity of the compounds Dr. Reitz asked Dr. Chamberlain to synthesize.

Dr. Chamberlain testified that he sent compounds he synthesized for "biological testing" (Exh. 2019 at, e.g., §5); however, we have not been directed to evidence establishing that:

(1) the "biological testing" was the Koboldt, Veenhuizen, or Anderson testing,

(2) that either Dr. Huang or Dr. Reitz explicitly or implicitly requested Dr. Chamberlain to have the "biological testing" performed, or

(3) that the "biological testing" established a practical utility for the compounds.

Of Koboldt, Veenhuizen, and Anderson, only Koboldt testified that she performed some testing (i.e., the testing of SC-58394) at the explicit request of one of the inventors,

i.e., Dr. Huang. We have not been pointed to evidence establishing that the other testing by Koboldt (i.e., the testing of SC-60246, SC-60247, SC-60248, SC-60667, and SC-60668) was done at the explicit or implicit request of an inventor. We have not been pointed to evidence establishing that any of the testing by Veenhuizen (i.e., the testing of SC-60246, SC-60247, SC-60248, SC-60667, and SC-60668) or any of the testing by Anderson (i.e., the testing of SC-60248) was done at the explicit or implicit request of an inventor. Since the evidence of record indicates that only Koboldt was working, at least in part, at either the explicit or implicit request of an inventor, i.e., Dr. Huang, only the work of Koboldt may inure to the benefit of the inventors under Genentech. Since the Koboldt testimony indicates that only the testing of SC-58394 was requested by Dr. Huang, only the testing of SC-58394 may inure to the inventors' benefit.

In reaching our decision, we assume--without deciding or finding--that the research laboratory in which the activities discussed above took place is probably a well-organized entity which undertakes legitimate scientific research in an orderly fashion. We further assume--without deciding or finding--that the individuals employed strive to achieve meaningful research goals consistent with the profit objectives of the company for

which they work. Consistent with our assumptions, we doubt that the employees operate as "independent contractors" each going their own way without meaningful direction from the head of the research laboratory. Nevertheless, our assumptions do not dispense with the need for credible evidence in the record of what occurred within a research laboratory. In other words, we cannot assume--unless there is credible evidence in the record--that (1) any particular individual discussed a problem with another individual, (2) any individual acted on behalf of another individual, or (3) any result obtained by one individual was communicated to another individual.

For example, even if we assume that Holtzman entered information said to have been provided to her into the research database, we do not know the precise significance of entry of the information. Furthermore, we do not know--unless there is evidence in the record--whether and when an individual might have consulted the database after entries were made therein. What remains a constant, however, is that we are bound to decide cases on the evidence and arguments before us--not a fact scenario which we imagine might exit.

The Koboldt testing of SC-58394

Koboldt testified that "testing showed compound SC-58394 to have good COX-2 inhibitory selectivity" and that she

"expected SC-58394 to have pharmacologically useful anti-inflammatory properties" based on test results (Exh. 2029 at ¶9). Koboldt summarized the COX-1/COX-2 assay in her testimony. Koboldt testified that the assay provides information on the ability of a compound to inhibit the activity of COX-2 relative to the compound's ability to inhibit the activity of COX-1. According to Koboldt, compounds that have COX-2 inhibition selectivity relative to COX-1 inhibition are considered to have pharmacologically useful anti-inflammatory properties (Exh. 2029 at ¶8).

The Order entered 11 January 2000, states the following (Paper 37 at 7):

> **j. Affidavits of expert witnesses**
>
> Affidavits expressing an opinion of an expert must disclose the underlying facts or data upon which the opinion is based. See Fed. R. Evid. 705 and 37 CFR §§ 1.639(b) and 1.671(b).
>
> Opinions expressed without disclosing the underlying facts or data may be given little, or no, weight. See Rohm and Haas Co. v. Brotech Corp., 127 F.3d 1089, 1092, 44 USPQ2d 1459, 1462 (Fed. Cir. 1997) (nothing in the Federal Rules of Evidence or Federal
> Circuit jurisprudence requires the fact finder to credit the unsupported assertions of an expert witness).

k. Reliance on scientific tests and data

Parties often rely on scientific tests and data, both in the preliminary motion phase and during the priority testimony phase. Examples include IR (infra-red spectroscopy) and graphs generated therefrom, HPLC (high performance liquid chromatography) and data generated therefrom, etc. In the event a party relies on a scientific test or data generated from a scientific test, the party relying on the test or data shall explain:

1. the reason why the test is being used and why the data is being relied upon;

2. how the test is performed;

3. how the data is generated using the test;

4. how the data is used to determine a value;

5. the acknowledged accuracy of the test; and

6. any other information which would aid the board in understanding the significance of the test or data.

See also 37 CFR § 1.671(f) and Notice of Final Rule, Patent Interferences Proceedings, 49 Fed. Reg. 48416, 48427-28, 48447 (col. 3) (Dec. 12, 1984).

In her testimony, Koboldt stated an opinion, i.e., that she expected SC-58394 to have good COX-2 inhibitory selectivity, without explaining or interpreting the data upon which the opinion is based. While Koboldt testified that she

recorded the results for SC-58394 in her notebook (Exh. 2038), Koboldt did not explain the meaning of the recorded results. For example, Koboldt did not explain how the values she obtained for
SC-58394 (found in pages of her notebook (Exh. 2038)), led her to conclude that SC-58394 had "good" COX-2 inhibitory selectivity (Exh. 2029 at ¶9). The recorded results Koboldt points to (at Exh. 2038) amount to fourteen pages of tables and graphs, none of which are explained in any detail by Koboldt.

Koboldt also testified that compounds having good COX-2 inhibitory selectivity "are considered to have pharmacologically useful anti-inflammatory properties" (Exh. 2029 at ¶9) and that "[a]t the time of the events described below, compounds having the ability to inhibit the activity of the COX-2 enzyme in vitro were understood to have anti-inflammatory utility predictive of their practical utility" (Exh. 2019 at ¶2). Evidence of *in vitro* activity in combination with a known correlation between *in vitro* and *in vivo* activity may be sufficient to establish a practical utility. Fujikawa v. Wattanasin, 93 F.3d at 1565, 39 USPQ2d at 1900; however, Koboldt's testimony does not credibly establish a known correlation between *in vitro* and *in vivo*

activity in COX-2 inhibitors. Koboldt gave no sufficient factual basis for the opinion that the *in vitro* results obtained for SC-58394 would have been predictive of anti-inflammatory activity *in vivo*. We have not been directed to other evidence of record establishing a known correlation between the *in vitro* activity Koboldt said she observed and *in vivo* activity in COX-2 inhibitors. We note that Huang does not supply any rebuttal evidence[3] in its reply brief (Paper 50) in response to Prasit's arguments that "the Huang record fails to establish any correlation between the Koboldt in vitro testing and any actual anti-inflammatory or analgesic utility clearly required for an actual reduction to practice" (Paper 49 at 16). Without further explanation on the record of the data obtained by Koboldt and the relationship between the *in vitro* testing done by Koboldt and *in vivo* utility, we can only speculate as to the significance of, and the weight to be given, the Koboldt testing. On this record, Huang has not shown by a preponderance of the evidence that the Koboldt testing established a successful reduction to practice of SC-58394.

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[3] We acknowledge Huang's arguments at Paper 50 at 13; however, the argument of counsel is not evidence. Estee Lauder Inc. v. L'Oreal, S.A., 129 F.3d at 595, 44 USPQ2d at 1615.

The other Koboldt testing and the Veenhuizen and Anderson testing

We hold that the following testing by Monsanto employees did not inure to the benefit of the Huang inventors:

(1) the Koboldt testing of SC-60246, SC-60247, SC-60248, SC-60667, and SC-60668 (Exh. 2029 at ¶¶10-14);

(2) the Veenhuizen testing (consisting of the *in vivo* testing of SC-60246, SC-60247, SC-60248, SC-60667, and SC-60668) (Exh. 2044 at ¶¶6-10); and

(3) the Anderson testing (consisting of the *in vivo* testing of SC-60668) (Exh. 2048 at ¶6).

However, even if the above testing did inure to the benefit of the Huang inventors, we hold that Huang has not shown that the testing established a practical utility for the tested compound. The Koboldt testimony regarding the testing of SC-60246, SC-60247, SC-60248, SC-60667, or SC-60668 suffers from the same deficiencies as the Koboldt testimony regarding her testing of SC-58394. The testing by Monsanto employees Veenhuizen and Anderson was directed to an *in vivo* utility; however, the testimony provided by the employees regarding the testing lacks an adequate explanation and interpretation of the results obtained. Each of the Monsanto employees drew the same conclusion regarding each compound tested (i.e., that

based on the test results obtained, the compound had pharmacologically useful anti-inflammatory activity (see Exh. 2029 at ¶11, Exh. 2044 at ¶11, and Exh. 2048 at ¶6)); however, none of them, in the testimony before us, adequately explained how the test results obtained support the conclusion drawn. None of the Monsanto employees analyzed the results so that we could understand why (or why not) the conclusion drawn was a valid one. It is not enough to simply point to the results obtained from said testing without further explanation (see e.g., Exh. 2048 at ¶6). We agree with Prasit that "[i]t is not the burden of the Board to try to read the exhibits and to correlate allegations made in the testimony with specific entries, i.e., the Board should not be expected to make highly technical conclusions without the benefit of clearly explained Exhibits" (Paper 49 at 22). For example:

(1) Veenhuizen points to pages of her notebook (Exh. 2047) where she testified she recorded the results of her testing. A review of the notebook pages reveals table after table of figures that apparently show either test conditions or test results. However, Veenhuizen does not adequately explain the significance of any particular figure or why a particular result led her to conclude that a particular

compound had pharmacologically useful anti-inflammatory activity.

(2) Anderson points to two pages of results he testified he recorded in his notebook (Exh. 2051) for SC-60668 and various other compounds that we assume are not within the scope of the count. However, we cannot be sure of the exact make up of the other compounds since we are not told. We cannot be sure of the significance of the figures for percentage inhibition for each tested compound since the formula used to obtain the figures is not adequately explained (e.g., the meaning of "ave. paw vol. Vehicle" is not explained). We note that some of the compounds yield a higher percentage of inhibition than does SC-60668 at either .3 or 2 mpk (e.g., 60583 at 3 mpk and Indo at .2 mpk). We also note that SC-60668 at .3 mpk yields a 4 percent inhibition while at 2 mpk the compound yields a 42% inhibition. However, we have not been provided with adequate testimony explaining the significance of the performance of SC-60668 relative to the other compounds tested or the significance of the dose of SC-60668 required to achieve 41 percent inhibition (e.g., is the dose pharmacologically practical?).

Therefore, even if we were to find that all the testing of SC-60246, SC-60247, SC-60248, SC-60667, or SC-60668 by the Monsanto employees inured to the benefit of the Huang inventors, Huang has not shown by a preponderance of the evidence that the testing established a successful reduction to practice of SC-60246, SC-60247, SC-60248, SC-60667, or SC-60668.

C. Conclusion

We deny Huang preliminary motion 1 for judgment that all the claims of the Prasit application are unpatentable to Prasit under 35 U.S.C. §§ 101 or 112, first paragraph as lacking an adequate description of utility and failing to be supported by an enabling disclosure.

We hold that Huang has not proven by a preponderance of the evidence that it actually reduced to practice an embodiment within the scope of the count prior to Prasit's constructive reduction to practice on 29 August 1994.

In particular, Huang has not shown that either inventor requested, either explicitly or implicitly, testing of SC-60246, SC-60247, SC-60248, SC-60667, or SC-60668 for the intended purpose of the invention. Therefore, the testing of the compounds by Monsanto employee Koboldt, Veenhuizen, or

Anderson did not inure to the benefit of the inventors under Genentech.

Furthermore, Huang has not proven by a preponderance of the evidence that the test results obtained by Monsanto employee Koboldt, Veenhuizen, or Anderson established a practical utility for SC-58394, SC-60246, SC-60247, SC-60248, SC-60667, or
SC-60668. Accordingly, even if the testing of SC-58394, SC-60246, SC-60247, SC-60248, SC-60667, or SC-60668 by the Monsanto employees inured to the benefit of the inventors, Huang has not shown that the inventors recognized a practical utility for any of the compounds sufficient to show an actual reduction to practice prior to 29 August 1994.

Superficially, our denial of Huang preliminary motion 1 and our holding that Koboldt's *in vitro* testing of compounds of the count did not establish a practical utility for the compounds prior to Prasit's constructive reduction to practice of 29 August 1994 may seem inconsistent. On the one hand, we deny Huang preliminary motion 1 attacking utility and enablement of the Prasit '931 claims while acknowledging that the '931 disclosure contains only *in vitro* testing of the claimed COX-2 inhibitors. On the other hand, we hold that Koboldt's *in vitro* testing of compounds of the count is

insufficient to establish a practical, i.e., *in vivo*, utility for the compounds. Our decision in both instances is based on the evidence brought to our attention and a recognition that Huang has the burden of proof both in its preliminary motion 1 (37 CFR § 1.637(a)) and in establishing priority of invention (37 CFR § 1.657(a)).

(1) As noted above, statements made by Prasit in its specification regarding utility and enablement are presumed correct unless there is reason to question the objective truth of those statements. Huang has the burden to show by a preponderance of the evidence that one having ordinary skill in the art would have doubted Prasit's assertion that the compounds it claims are useful as COX-2 inhibitors. We note that Huang does not attack the sufficiency of the *in vitro* testing found in the '931 disclosure and states that it disagrees with Merck testimony in other interferences indicating that, in some cases, *in vitro* activity alone is insufficient to make reliable predictions concerning *in vivo* effectiveness of compounds alleged to possess anti-inflammatory, antipyretic and analgesic activity (Paper 47 at 4). Huang argues that Prasit should be held to the Merck testimony from the other interferences in this interference under principles of estoppel even though Huang disagrees with

the testimony. We hold that there is no estoppel since the Merck testimony was limited to compounds found in application not involved in the present interference. We have no reason to further examine the sufficiency of the testing relied upon by Prasit to establish utility and enablement in the '931 application because Huang has not otherwise challenged those tests. Huang has not shown that the *in vitro* testing of the Prasit '931 application would have been inadequate for purposes of enablement and utility of the '931 claims.

(2) To establish priority, Huang relies, in part, upon *in vitro* testing done by Koboldt. Huang has the burden of proving an actual reduction to practice of an embodiment of the count, which includes recognition of a practical utility for the embodiment, prior to Prasit's constructive reduction to practice date of 29 August 1994. As noted above, evidence of *in vitro* activity in combination with a known correlation between *in vitro* and *in vivo* activity may be sufficient to establish a practical utility; however, Koboldt's testimony does not credibly establish the basis for her opinion that there a known correlation between *in vitro* and *in vivo* activity in COX-2 inhibitors, either generally or for the compounds of the count. Accordingly, Huang has not shown that

Koboldt's testing established a practical utility for the tested compounds.

II. Order

Upon consideration of the record of the interference and for reasons given, it is

ORDERED that Huang preliminary motion 1 is DENIED;

FURTHER ORDERED that judgment on priority as to Count 1, the sole count in the interference, is awarded against junior party HORNG-CHIH HUANG and DAVID B. REITZ;

FURTHER ORDERED that junior party, HORNG-CHIH HUANG and DAVID B. REITZ, is not entitled to a patent containing claims
1-18 of application 08/541,850, which correspond to Count 1;

FURTHER ORDERED that a copy of this decision be given a paper number and be entered in the administrative records of Huang's 08/541,850 application and Prasit's 08/793,931 application.

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Administrative Patent Judge)
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RICHARD E. SCHAFER)
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)
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